**Fatal outcome of Intravenous injection of Benzathine Penicillin G in a neonate-case report**

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***Abstract***

*Acute reactions simulating anaphylaxis have been reported after intravenous injections of aqueous procaine penicillin G. Here I report a case of two neonates in whom the classical "pseudoanaphylactic" reactions occurred after inadvertent administration of Benzathine Penicillin G by intravenous infusion. Cardiorespiratory arrest with slow idioventricular rhythm was observed within a few minutes of the infusion in one of the neonate and passed away, the other neonate was observed to experience several episodes of convulsions and manage to survive. Microembolization to the lungs and brain, as well as direct toxicity from the procaine component of aqueous procaine penicillin G, are probably the pathogenic mechanisms. This case report draws the attention of nurses and mid wives to be more vigilant and establishes protocol of how to avoid intravenous injections of Benzathine penicillin G.*

Benzathine Penicillin G is a commonly prescribed antibiotic in neonates born from mothers who are diagnosed of sexually transmitted disease during prenatal screening. It is given intramuscularly after dermal test dose is done. Yet report of overdose or death with this drug is not common. We report two cases in which the neonates developed complications following intravenous injection of Benzathine Penicillin , one developed cardiac arrest within an hour of intravenous injection and died shortly and the other one survived several episodes of convulsions1 (fits) and a prolong stay in the neonatal Intensive care unit

Benzathine Penicillin G is a medicine which should be given strictly intramuscularly and in both these cases it was given intravenously by ignorance or by negligent by a midwife.

**Keywords**: Benzathine Penicillin G, cardiac arrest, seizures

**Case History**

Twopregnant mothers were admitted to the prenatal ward of Victoria Hospital. Both were diagnosed of TPHA positive during antenatal care and treatment were given to both mothers. Both babies were born by normal deliveries which were uneventful. The treating paediatrician has stared Penicillin G with both the babies after test dose. Benzathine penicillin G were given two both babies by intramuscular route by competent nurses. However on the termination of the treatment, the last dose of Benzathine Penicillin G was given intravenously to both the babies by a new midwife. The immediate lost of consciousness by one of the babies was noticed by the nurse and the mother, the baby was taken immediately to the neonatal ICU, resuscitation started but in vain.

The baby was declared dead.

The other baby started getting convulsions and was also transferred to Neonatal ICU, treatment started immediately and the baby survived

**Description.**

Penicillin G benzathine and penicillin G procaine injectable suspension contains equal amounts of the benzathine and procaine salts of penicillin G4. It is available for deep [intramuscular](https://www.rxlist.com/script/main/art.asp?articlekey=4012)injection.

Penicillin G benzathine is prepared by the reaction of dibenzylethylene diamine with two molecules of penicillin G. It is chemically designated as (2S,5R,6R)-3,3-Dimethyl-7-oxo-6-(2phenylacetamido)-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid compound with N,N'dibenzylethylenediamine (2:1), tetrahydrate. It occurs as a white, crystalline powder and is very slightly soluble in water and sparingly soluble in alcohol. Its chemical structure is as follows:

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| Bicillin® C-R (penicillin G benzathine and penicillin G procaine injectable suspension) Structural Formula Illustration |

Penicillin G procaine, (2S,5R,6R)-3,3-Dimethyl-7-oxo-6-(2-phenylacetamido)-4-thia-1azabicyclo[3.2.0]heptane-2-carboxylic acid compound with 2-(diethylamino)ethyl paminobenzoate (1:1) monohydrate, is an equimolar salt of procaine and penicillin G. It occurs as white crystals or a white, microcrystalline powder and is slightly soluble in water. Its chemical structure is as follows:

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| Bicillin® C-R (penicillin G benzathine and penicillin G procaine injectable suspension) Structural Formula Illustration |

Each disposable syringe (2 mL size) contains the equivalent of 1,200,000 units of penicillin G comprising: the equivalent of 600,000 units of penicillin G as the benzathine salt and the equivalent of 600,000 units of penicillin G as the procaine salt in a stabilized aqueous suspension with sodium citrate.

**Autopsy**

An autopsy was carried on the unfortunate baby. The autopsy did not reveal much, except congestion of all organs and no congenital malformation. The cause of death was acute pulmonary oedema. Blood sample were sent to the FSL for toxicological analysis and organs were sent for histopathology.

No significant pathology were noted on microscopic examination

The toxicological analysis of the blood reveal the presence of Benzathine Penicillin, same was also confirmed from the suspected vial which was used by the midwife.

**Discussion**

Crystalline penicillin is usually preferred in neonates when penicillin is indicated. Procaine penicillin is recommended as an alternative to crystalline penicillin especially for infections like congenital syphilis and neonatal sepsis. Procaine penicillin may be more practical for the community management of neonatal sepsis because of the once daily dosing schedule, cost, availability and ease of administration5. However, there is paucity of data on the efficacy and safety in such settings. This drug has been in use for several decades and there are very few reports on adverse events in the neonate.

Most WHO guidelines recommend crystalline penicillin as the first choice in neonates, when penicillin is indicated. Reports on adverse events in neonates are few, especially when the correct dose and the proper route of administration is used. In neonates, infants, and small children, injection into the midlateral muscles of the thigh is preferred6.

Penicillin G benzathine must be administered by the intramuscular (IM) route only and should never be administered via intravenous route. Special precautions should be taken to avoid intravascular injection. Avoid intramuscular injection of these suspensions near major nerves or blood vessels because this could cause neurovascular damage. There have been reports of inadvertent intravenous administration of penicillin G benzathine which has been associated with cardiorespiratory arrest and death.

The most likely pathophysiologic explanation for these fatalities is that the Benzathine Penicillin G compound is a crystalline powder that may cause direct damage when injected into a blood vessel, possibly eliciting vascular spasm and subsequent occlusion by the large crystals of the penicillin salt7

[Penicillin](https://www.rxlist.com/script/main/art.asp?articlekey=15277) in over dosage has the potential to cause [neuromuscular](https://www.rxlist.com/script/main/art.asp?articlekey=34038) hyperirritability or convulsive seizures.

**Conclusion and recommendation**

Although the exact cause of her cardiac arrest was not known, the most likely cause was probably due to due intravenous bolus injection of Benzathine Penicillin, as inferred from the presence of Benzyl Penicillin in the deceased blood. Moreover both the neonates were given intravenous injections by the same nurse and prepared from same vial and both developed complications immediately. No other medication was given at that time.

Fatal non-allergic reactions to Benzathine Penicillin G may occur as quickly as a few minutes following administration.

This report should encourage healthcare professionals to administer Benzathine Penicillin G only when clearly indicated and to be prepared for life-threatening situations.

This medication must not be injected into a vein or mixed with solutions that will be injected into a vein.

Before using, check the product visually for particles or discoloration. If either is present, do not use the liquid.

Learn how to store and discard medical supplies safely.

Do not share this medication with others.

Properly discard the product when it is expired or no longer needed.

In case of emergency, contact a [poison control](https://www.medicinenet.com/poison_control_centers/article.htm) centre or emergency room immediately

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